

REMARKS

Claims 19-39 were previously pending in this application. Claims 19-39 are still pending for examination with claim 19 being an independent claim. No claims have been amended, canceled or added. No new matter has been added.

Double Patenting Rejection

Claims 19-39 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 42-47, 49-53, 56, 57, 82-85, 90, 92, 94, 96, 98, 100, 102 and 103 of co-pending Application No. 09/337584. Applicants note that the claims of U.S. 09/337584 were in allowable condition and are currently in an Interference. Applicants will consider filing a terminal disclaimer if the claims are allowed after the Interference.

Claims 19-39 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 46, 52, 64, 71, 72, 74 and 80 of co-pending Application No. 10/613739. Applicants note that U.S. 10/613739 is not commonly owned with the instant patent application. Further, U.S. 10/613739 is later filed. If the claims are obvious over the instant claims, with which Applicants disagree, the rejection should be maintained in that case and the instant claims should be allowed to grant.

Claims 19-39 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 22, 23, 31, 32 and 34-37 of co-pending Application No. 10/769282. Claims 19-39 also have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 19-29 and 31-33 of co-pending Application No. 10/894862. It is requested that the rejection be held in abeyance until allowable subject matter in any of the cited applications is identified.

Claims 19-39 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 42, 45-53, 57-60 of co-pending Application No. 09/337893. The cited application is abandoned. Thus, it is requested that the rejection be withdrawn.

The Examiner has maintained the provisional obviousness-type double patenting rejection over 09/337584, 10/613739, 10/769282, 10/894862 and 10/337893. The Examiner also pointed out that Applicants allegedly did not address the provisional obviousness-type double patenting rejection over 10/769282. Applicants addressed this rejection in the response to the Office action dated April 24, 2006, but it was inadvertently left out of Applicants' response dated April 15, 2007. It is addressed herein.

Rejection Under 35 U.S.C. 112

Claims 19-39 have been rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The Examiner states that the claims do not define the structure of the immunostimulatory oligonucleotide. Applicants respectfully disagree. Initially, Applicants point out that the rejection does not refer to any dependent claims. Dependent claims 21-27 provide further structural limitations on the CpG oligonucleotide. For instance, claims 23-25 are limited to oligonucleotides including a specific sequence such as AACGCTCG, AACGTT, AGCGTC, GACGTT, GACGTC, AACGTT, and AGCGTT. Claims 26 and 27 recited specific formulas. Claim 21 requires that the CpG motif be flanked by two purines on the 5' side and two pyrimidines on the 3' side. Claim 22 adds the limitation that the oligonucleotide includes at least two CG dinucleotides. No reasons are provided for why such structural limitations are insufficient to meet the written description requirement.

Claim 19 recites an oligonucleotide that has an immunostimulatory motif. The immunostimulatory motif consists, at a minimum, of a CG dinucleotide. Applicants discovered that a CG dinucleotide conferred immunostimulatory properties on an oligonucleotide. The data

in the specification established that disruption of this core motif abolished immunostimulatory activity. The claims recite the minimal elements essential for activity in the method. One skilled in the art would recognize based on the discoveries of the invention that Applicants had possession of an oligonucleotide minimally composed of a CG dinucleotide for the treatment of asthma.

The specification provides an adequate description to support such a claim. Immunostimulatory nucleic acid molecule is defined in the specification on Page 14. An “immunostimulatory nucleic acid molecule” refers to a nucleic acid molecule, which contains an unmethylated cytosine, guanine dinucleotide sequence and stimulates an immune response, for example has a mitogenic effect on, or induces or increases cytokine expression by a vertebrate lymphocyte. The specification also provides that “preferably, the immunostimulatory CpG DNA is in the range of between 8 to 40 base pairs in size if it is synthesized as an oligonucleotide.” Applicants provide numerous examples of immunostimulatory nucleic acid molecules throughout the specification, in the Figures, and in the Examples. Applicants provide numerous sequences of immunostimulatory nucleic acid molecules comprising CG. Applicants define the critical motif, CG, and identify and describe the structure-function relationship in multiple assays. Based on Applicants’ disclosure a person of ordinary skill in the art would have no problems envisioning the structure of individual species making up the claimed genus and would understand that there is the potential of generating many possible immunostimulatory nucleic acid molecules with considerable divergence regarding the nucleic acid sequence.

The Examiner has stated that claim 19 recites six or more nucleotides. Applicants note that claim 19 does not specify this element. Claim 21, dependent on claim 19, recites that the immunostimulatory motif comprises a CG flanked by two 5’ purines and two 3’ pyrimidines. The term “comprises” in claim 21 allows for a minimum of six nucleic acids, but encompasses longer oligonucleotides, for example 8 nucleotides, or more. The Examiner states on pages 6 and 11 that “Applicants’ specification indicates that ODNs shorter than 8 bases were non-stimulatory (p. 19, 1. 4-5).” The specification, on page 18, lines 30-31, actually teaches that “of

those tested, ODNs shorter than 8 bases were non-stimulatory,” rather than teaching that they do not work.

It is further noted that claim 19 recites the limitation that any oligonucleotides falling in the scope of this claim must be “immunostimulatory,” thus excluding oligonucleotides if they are not immunostimulatory. Therefore, the scope of claim 19 is fully consistent with, and supported by what is presented in the specification, and hence claim 19 and claims dependent thereon do not lack written description.

Yamamoto et al. (1994) was cited to support the position that relatively short oligonucleotides are inactive. Applicant respectfully contends that the teaching of the Yamamoto reference is taken out of its context. In the Brief Communication, Yamamoto et al. examined 13 oligonucleotides of various length, in the context of the AACGTT hexamer. Among the 13 oligonucleotides tested, only three were 16 nucleotides or less in length. Based on this, the authors concluded “the oligonucleotides 16 bases or less in length were not active” (abstract). Given the limited scope of the study, such conclusion should be construed only in the narrow context in which the study was conducted. The data presented in Yamamoto et al. are insufficient to support a broad notion that *no* oligonucleotides 16 or shorter in length are immunostimulatory, as suggested by the Examiner. Indeed, later evidence suggests otherwise. For example, specific examples of immunostimulatory CpG oligonucleotides that are 6 nucleotides or shorter are described in U.S. Patent Application 11/361313 (see, for example, Table 3), which teaches oligonucleotides of 2 to 7 nucleotides in length. Thus, the evidence is sufficient to rebut the teachings of Yamamoto et al. to the extent that they are viewed as supporting a lack of written description.

Based on the arguments above Applicants kindly request the Examiner to reconsider these rejections and to withdraw them.

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CONCLUSION

A Notice of Allowance is respectfully requested. The Examiner is requested to call the undersigned at the telephone number listed below if this communication does not place the case in condition for allowance.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, that is not covered by an enclosed check, please charge any deficiency to Deposit Account No. 23/2825 (C1039.70073US00).

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Respectfully submitted,

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